REMARKS

The Office Action mailed January 24, 2006, has been received and reviewed. Claims 1 and 3-22 are currently pending in the application. Claims 1, 3-8, 11, 13, 15, 16 and 22 stand rejected. Claims 9, 10, 12, 14 and 17-21 have been cancelled herein. Applicants propose to amended claims 1, 3-8, 11, 13, 16 and 22. All amendments and cancellations have been made without prejudice or disclaimer. Applicants respectfully request reconsideration of the application as amended.

Double Patenting

Claims 1-8, 11, 13, 15 and 22 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as assertedly being unpatentable over claims 1-5, 7, 12, 14 and 16 of co-pending application no. 10/303,157 (the '157 application), in view of U.S. Patent 5,885,779 and further in view of Nicholson *et al.* More particularly, while acknowledging that the '157 application teaches a chimeric receptor that is default inactive unless bound by ligand and prey, the Examiner maintains that it would have been obvious to substitute the gp130 cytoplasmic domain from Nicholson for the cytoplasmic domain of the receptor from the '157 application.

Obviousness-type double patenting relies on the same standard as set forth for an obviousness rejection under 35 U.S.C. § 103. *In re Braat,* 937 F.2d 589, 19 USPQ2d 1289 (Fed. Cir. 1991); *In re Longi,* 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). M.P.E.P. § 804. To establish and maintain a *prima facie* case of obviousness under 35 U.S.C. § 103 there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or combine reference teachings. Also, there must be a reasonable expectation of success and the prior art reference (or references when combined) must teach or suggest all the claim elements.

The double patenting rejection is improper because a *prima facie* case of obviousness has not been established against claims 1, 3-8, 11, 13, 15 and 22 in view of the cited references. In particular, there would be no motivation to combine or expectation of success to use the system

described by the Examiner because it would not work as proposed.

In Nicholson, the SOCS3 inhibitory action is demonstrated to be caused by SOCS3 directly binding to a docking site on the cytoplasmic domain of gp130 (Nicholson, p. 6493). However, it is a claim element in the instant claims for the inhibitor to be brought to the activation site by a heterologous bait-prey interaction; not by an inhibitor-docking site interaction. (*See, e.g.*, independent claims 1 and 22).

In the system proposed by the Examiner, disruption of the bait-pray interactions would not lead to activation of the receptor, as SOCS3 would still keep its affinity to the docking site on gp130, and inhibit the receptor activation. Only if both the bait-prey interaction and SOCS3 docking-site interaction could be disturbed would a positive activation signal be seen. As such, there would be no motivation to combine the cited references because the system as proposed by the Examiner would not screen for an interaction between a bait polypeptide and a prey polypeptide as taught by the instant application.

Furthermore, the inhibition of the receptor by the bait-prey interaction needs to be very high and consistent. One of ordinary skill in the art would not expect that an inhibitor-prey fusion construct would be efficient enough to inhibit nearly 100% of the activation by a bait-prey interaction. It is clear from Nicholson that the receptor inhibition is not very efficient, and that only high expression of SOCS3 can block the receptor activation (Nicholson, p. 6493, col. 2). As such, a person or ordinary skill in the art would assume that, when the inhibitor is recruited by a bait-prey interaction, and not by a direct inhibitor-docking site interaction, the inhibition would be less effective, and the signal/noise ratio would be insufficient to screen for disruptors.

Therefore, the obviousness-type double patenting rejection is improper as the cited references do not support a *prima facie* case of obviousness because there is no motivation to combine the references as suggested and there is no expectation of success to combine the references and use the system as proposed by the Examiner.

Consequently, it is respectfully requested that the provisional obviousness-type double patenting rejection of claims 1, 3-8, 11, 13, 15 and 22 be withdrawn.

Claim rejections—35 U.S.C. § 102(b)

Claims 1, 3-5, 11, 13, 15, 16, and 22 are rejected under 35 U.S.C. § 102(b) as allegedly

being anticipated by Medici *et al.*, 1997 (The EMBO Journal. 16(24): 7241-7249). However, a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single reference which qualifies as prior art under 35 U.S.C. § 102. *Verdegaal Brothers v. Union Oil Co. of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Applicants traverse this rejection and respectfully submit that Medici fails to disclose each and every element of the rejected claims.

Amended claims 1, 16 and 22, as proposed to be amended, recite, in part, a recombinant mammalian receptor. However, Medici only discloses a recombinant yeast receptor. As such, Medici does not disclose each and every element of amended claims 1, 16 and 22 and the claims dependent therefrom.

Furthermore, amended claims 1 and 22, as proposed to be amended, comprise a cytoplasmic domain including at least one activation site. Medici does not expressly or inherently teach a cytoplasmic domain including at least one activation site. In fact, the GPCRs of Medici do not have any activation sites on the cytoplasmic domain—the activation site of the GPCRs is on the G-protein. Furthermore, applicants respectfully affirm that those of ordinary skill in the art will understand that an activation site is a site limited to one or a few amino acids. Such an activation site is not undergoing a conformational change as taught by Medici. When speaking of a protein conformational change, a person of ordinary skill in the art would understand that the change is in reference to a change in a protein domain and not an activation site.

Applicants respectfully submit that, according to the understood definition of an activation site, and as demonstrated by the examples of the referenced application, that modification of a conventional activation site refers to *enzymatic modifications,* and does not include conformational changes which are not *first* induced by an enzymatic modification.

The Examiner asserts that the GTP/GDP exchange meets the definition of modifying enzyme activity. However, it is stated that the modifying enzyme activity is modifying the activation site, and the activation site should be situated on the receptor chain. This condition is not fulfilled in Medici because, as discussed previously, the GPCRs of Medici do not have any activation sites on the receptor's cytoplasmic domain.

Additionally, the Examiner asserts that the claim 1 element reciting "wherein the activation of said recombinant receptor is inhibited by binding of a fusion protein to said heterologous bait polypeptide" is an inherent feature of the receptor described by Medici. However, amended claim 1, as proposed, includes a mammalian recombinant receptor which is not expressly or inherently taught by Medici. Furthermore, the assertion may only be true when both an active prey fusion protein and an inactive prey fusion protein are present. Note that the definition of "inhibition of activation" states that the *receptor is activated in absence of the binding* (Specification, paragraph [0057]). However, in the Examiner's interpretation, the receptor can only be activated *by binding of another fusion protein.*

For the foregoing reasons, applicants respectfully submit that Medici does not expressly or inherently disclose each and every element of amended claims 1, 16 and 22, as proposed to be amended herein. Furthermore, claims 3-5, 11, 13, 15 should be allowable, *inter alia*, as depending from amended independent claim 1.

Applicants respectfully request withdrawal of the 35 U.S.C. § 102(b) rejection of claims 1, 3-5, 11, 13, 15, 16, and 22.

Claim rejections—35 U.S.C. § 103(a)

The Examiner maintains that claims 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Medici *et al.* in view of Osborne *et al.* Applicants respectfully traverse the rejections as hereinafter set forth.

A *prima facie* case of obviousness cannot be established because Medici and Osborne, fail to teach or suggest every claim element since claims 6-8 depend from and, thus, include the elements of amended, base claim 1. On page 8 of the Office Action, the Examiner acknowledged that Medici and Osborne both use yeast proteins and yeast cells. However, amended independent claim 1, as proposed to be amended, includes a recombinant mammalian receptor. Accordingly, applicants submit that Medici and Osborne, alone or in combination, fail to teach or suggest a recombinant mammalian receptor as required by the proposed amended claim 1.

Therefore, claims 6-8, dependent from claim 1, are not obviousness in view of Medici and Osborne. Reconsideration and withdrawal of the obviousness rejection is requested.

Entry of Amendments

It is respectfully requested that the proposed claim amendments be entered. The proposed amendments merely place the claims in condition for allowance and do not introduce new matter into the application, nor would they require any additional search. Support for amending the claims to include a recombinant mammalian receptor may found, *inter* alia, in paragraph [0024] and the examples in the specification. In the event that a decision is made not to enter the proposed claim amendments, entry thereof upon the filing of a Notice of Appeal in the above-referenced application is respectfully requested.

CONCLUSION

In view of the foregoing proposed amendments and remarks, the applicants submit the claims define patentable subject matter and a notice of allowance is requested. Should questions remain after consideration of the foregoing, the Office is kindly requested to contact the applicants' attorney at the address or telephone number herein.

Respectfully submitted,

Yury M. Colton, Ph.D.
Registration No. 55,081
Attorney for Applicants
TRASKBRITT, P.C.
P.O. Box 2550
Salt Lake City, Utah 84110-2550
Telephone: 801-532-1922

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